PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 3 : B04B 1/10, 1/12, 11/02 — A1

(11) International Publication Number: WO 85/ 02561

(43) International Publication Date: 20 June 1985 (20.06.85)

(21) International Application Number: PCT/US84/01796

(22) International Filing Date: 5 November 1984 (05.11.84)

(31) Priority Application Numbers: 560,946; 560,987

(32) Priority Dates: 13 December 1983 (13.12.83); 13 December 1983 (13.12.83)

(33) Priority Country: US

(71) Applicant: BAXTER TRAVENOL LABORATORIES, INC. [US/US]; One Baxter Parkway, Deerfield, IL 60015 (US).

(72) Inventor: BROWN, Richard, I. ; 2335 Peachtree Lane, Northbrook, IL 60062 (US).

(74) Agents: RYAN, Daniel, D. et al.; One Baxter Parkway, Deerfield, IL 60015 (US).

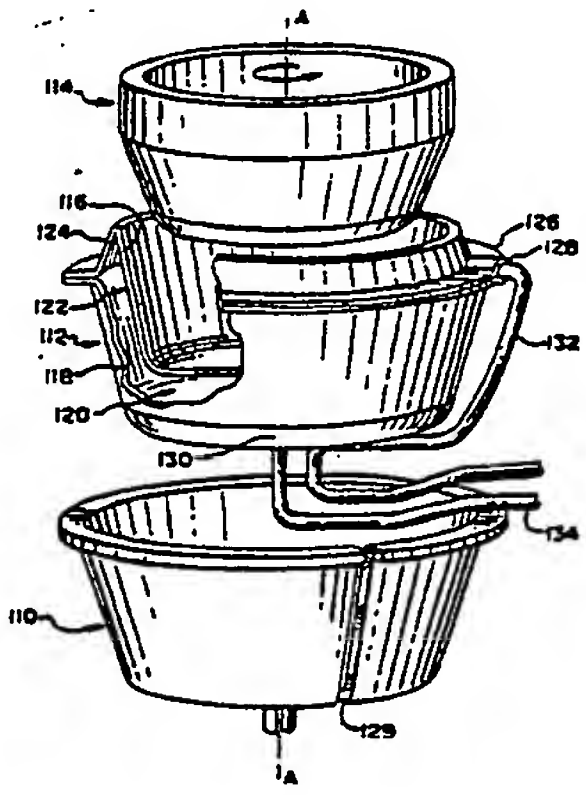
(81) Designated States: BE (European patent), DE (European patent), FR (European patent), GB (European patent), JP.

Published
With international search report.

(54) Title: FLEXIBLE DISPOSABLE CENTRIFUGE SYSTEM

(57) Abstract

A bowl-shaped chamber for use in centrifugal apheresis. The chamber is used for receiving whole blood, separating blood into therapeutic components and selectively collecting the therapeutic components. In one embodiment, the chamber (10) includes a bladder-like casing, which is formable into a bowl-like chamber having a bowl-shaped outer wall (32) and a bowl-shaped inner wall (34). The inner and outer walls (32, 34) define a blood processing cavity (37) therebetween and a flexible rim area (40) connects the inner and outer walls. The rim area (40) defines a rim edge (34c) and the bowl is substantially symmetric about a central spin axis. The rim area (40) is adapted to fold against itself so as to form the rim edge (34) which is adapted to advance and retract as the chamber volume changes. In another embodiment, the bowl (112) has inner and outer walls (116 and 118) which define bottom and side walls sections (120 and 122), a blood receiving cavity between said walls, and at least one port (128, 130) for fluid communication with said cavity. The bowl bottom section (120) defines a cylindrically-shaped plasma processing volume (136) and the side wall section defines an annularly-shaped red blood cell processing volume (140). The red blood cell processing volume (140) and the plasma processing volume (136) are approximately equal.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GA	Gabon	MR	Mauritania
AU	Australia	GB	United Kingdom	MW	Malawi
BB	Barbados	HU	Hungary	NL	Netherlands
BE	Belgium	IT	Italy	NO	Norway
BG	Bulgaria	JP	Japan	RO	Romania
BR	Brazil	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic			SE	Sweden
CG	Congo	KR	Republic of Korea	SN	Senegal
CH	Switzerland	LI	Liechtenstein	SU	Soviet Union
CM	Cameroon	LK	Sri Lanka	TD	Chad
DE	Germany, Federal Republic of	LU	Luxembourg	TG	Togo
DK	Denmark	MC	Monaco	US	United States of America
FI	Finland	MG	Madagascar		
FR	France	ML	Mali		

FLEXIBLE DISPOSABLE CENTRIFUGE SYSTEM

BACKGROUND OF THE INVENTION:

This invention relates to a centrifugal liquid processing apparatus, and more particularly, to a novel processing or separation chamber and system for use in centrifugal apheresis (e.g., plasmapheresis or plateletapheresis).

In recent years long-term storage of human blood has been achieved by first obtaining whole blood from a donor at a collection center and, thereafter, separating the blood into therapeutic aomponents, such as plasma, platelets, and red cells at a central processing laboratory. The separated components are then collected and stored for future use.

The separation of the blood into constituent components is typically performed using a centrifuge or centrifugal liquid processing apparatus. Such systems are disclosed in U.S. Patents 3,987,961; 4,132,349; and 4,285,464. In such systems the processing chamber into which the whole blood is delivered for separation has in general been bowl-shaped, rigid and usually disposable. A number of different fluid connection systems are known for connecting the rotating processing chamber to external stationary blood sources or

component collection containers. Some of these systems use stationary rather than rotating seals. See, for example, U.S. Patent 4,151,844; 4,285,464; and 4,389,207.

In addition to central processing laboratories, newer systems are being developed in which the centrifuge is located at the collection center and the donor is connected to the processing apparatus during the donation, separation and collection operations. A number of advantages are recognized from such systems, such as speed of collection, increased component yield, reduced cost, and the like.

It has been determined that in the newer systems it is particularly desirable that the volume of the separation chamber be variable so as to accommodate those volume changes occurring during the separation and collection procedures. Furthermore, the chamber should be one-piece and removable from the centrifugal processing apparatus for transporting of blood or components within the chamber.

In addition, the chamber should be sterilely sealed to external sites such as component collection bags and catheters. Desirably, the entire system should be integral and disposable.

It is also desirable to provide a processing chamber which is less expensive to manufacture than the existing bowl systems.

It is therefore an object of this invention to provide a one-piece, variable-volume processing chamber which can be economically manufactured and which may be part of a complete collection and separation system.

In the processing of blood, it is generally desirable to first separate red blood cells from the whole blood and thereafter separate and collect platelets from the remaining plasma. It is also desirable to maximize platelet collection in general and, more specifically, to maximize collection of platelets which may be associated with the red blood cells.

During centrifugal processing the red blood cells separate or sediment against the bowl wall. In existing bowls the plasma forms a layer inwardly of and adjacent the red blood cell layer with an interface of "buffy layer" of platelets forming therebetween. In such a situation three adjacent layers are formed: the red blood cell layer, the platelet or buffy layer, and the plasma layer. However the discreteness of the layers may not be as precise as desired.

Thus when collecting the components, it may be difficult to precisely separate each component without including another component. For example, some platelets may be collected during collection of the red blood cells. Thus separation and collection of the components will not have been maximized.

It is particularly important in collecting platelets to maximize the collection of platelets from whatever quantity of blood is taken from the donor. To this end it is believed to be desirable to minimize the separation of platelets from plasma during the separation of red blood cells.

It is therefore an object of this invention to provide a processing chamber which is shaped to assure maximum separation of red blood cells while also minimizing platelet separation.

These and other objects of this invention will become apparent from the following description and appended claims.

SUMMARY OF THE INVENTION

There is provided herein a flexible, one-piece, variable-volume processing chamber for use in centrifugal apheresis (e.g., plasmapheresis or plateletapheresis) which can be easily and economically manufactured. The chamber is useful in receiving whole blood, separating the blood into therapeutic components, and the selective collection of such components.

The chamber includes a flexible, bladder-like casing which is formable to a bowl-like shape having an outer wall and an inner wall which when spaced from each other define the blood-receiving and processing cavity. A flexible rim area connects the inner and outer walls and defines a flexible rim edge. The resulting bowl is substantially symmetric about a central spin axis, is flexible, and the rim area is constructed to fold or lay against itself and to roll in an axial direction or advance and retract as the chamber is filled and emptied. At least one port provides fluid communication between the flood-receiving cavity and external sites.

The chamber may be one component of an integral sterile and disposable separation and collection system which also includes fluid-carrying tubing, collection bags, and a catheter.

There is also disclosed herein an enclosed processing bowl for use in centrifugal apheresis which minimizes platelet separation during red blood cell separation and collection and which maximizes platelet collection by maximizing the blood sedimentation surface area and minimizing the buffy layer interface area.

The bowl has inner and outer walls which define bottom and side wall sections, a blood receiving cavity between said walls, and at least one port for fluid communication with said cavity. The bowl bottom section defines a cylindrically-shaped plasma processing volume, and the side wall section defines an annularly-shaped red blood cell processing volume. The red blood cell processing volume and the plasma processing volume are approximately equal.

The plasma processing volume and red blood cell processing volume form a generally cylindrical interface at the transition from the bottom section to the side wall section. The buffy layer forms at this interface.

The outer wall of the side wall section forms a red blood sedimentation surface and the area of the sedimentation surface is greater than the surface area of the blood cell/plasma interface.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGURE 1 is a perspective view showing the flexible, variable-volume, bowl-shaped chamber with mating parts of a centrifugal processing apparatus;

FIGURE 2 shows the bowl-shaped chamber distended to show the bladder-like casing shape and show how the bowl-shaped chamber is formed;

FIGURE 3 shows a rim edge and a portion of the rim area rolled back upon itself in advanced and retracted positions;

FIGURE 4 shows another version of the chamber with the rim edge;

FIGURE 5 through FIGURE 12 show the operation of a centrifuge system using the bowl-shaped chamber;

FIGURE 13 shows a integral sterile and disposable separation and collection system.

FIGURE 14 is a perspective view showing a processing apparatus and variable volume bowl;

FIGURE 15 is a sectional and perspective view showing a fully filled bowl and the red blood cell and the plasma volumes;

FIGURE 16 is a sectional and perspective view showing a partially filled bowl and the red blood cell and the plasma volumes;

FIGURE 17 is a perspective view, partially in section, showing a fixed volume and the red blood cell and the plasma volumes.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring now to Figure 1, a flexible, variable-volume, bowl-shaped processing chamber 10 generally is shown positioned between a bowl-shaped rotor 12 and a conformingly-shaped and movable mandrel 14.

As previously indicated, centrifugal liquid processing apparatus of the type used in centrifugal apheresis are known in the art. Drive systems for spinning the separation chambers, speed

control systems, and the like, are also known in the art. Those systems are not shown herein as they are known in the art, and as this invention is directed to the flexible, variable-volume chamber and the system of which it may be a part.

The rotor bowl 12 includes a bottom wall portion 16, upwardly-extending side wall 18, an upper lip or edge 20, a tube-receiving slot 21, and is generally symmetric about a vertical spin axis 22-22. The rotor bowl also includes at least one port or passageway 24, which is located in the bottom wall 16 at the spin axis 22-22.

The flexible chamber 10 is constructed to fit within the rotor bowl 12 for rotation therewith, and the chamber may have a shape which is generally complementary to that of the rotor bowl.

The mandrel 14 is a cup-shaped member, similar in shape to the rotor bowl 12, and is adapted to nest therein. The mandrel 14 includes a bottom wall 26, an upwardly-extending side wall 28, and skirt 30. The mandrel is axially movable toward and away from the chamber 10 so that the chamber's volume may be controlled by the cooperation of the mandrel 14 and rotor bowl 12. The mandrel is mounted to the processing apparatus so as to spin with the rotor bowl 12 and the chamber 10 about axis 22-22.

The flexible chamber 10, as shown herein, includes an outer wall 32 and an inner wall 34 which are joined along a flange or shoulder-like seal 36 to form an enclosed casing. The space between the walls defines a blood-receiving cavity 37.

The inner and outer walls, as shown here, are formed of a flexible, medical-grade, polymeric material, such as polyvinylchloride. In the preferred embodiment, the walls are sealed, flexible and pliable. The outerwall 32 includes a fluid port 38 and integral conduit 39, which provides fluid communication between the cavity 37 and external blood sources or therapeutic component collection sites. The port 38 is shown as aligned with

the spin axis and forms what is known as the low-gravity or low-G port. The inner wall 34 is shown as depressed inwardly toward the outer wall 32 and forming a rim area 40 generally adjacent the flange 36.

As can be seen in Figure 1, the flexible processing chamber 10 fits within the rotor bowl 12, and since it is flexible, the outerwall 32 will conform to the shape of the rotor wall when the chamber is filled and spinning. The conduit 39 and port 38 are positioned in the cover 12 through the slot 21. The mandrel 14 fits within the depression or space formed in the inner wall 34, and the inner wall 34 will conform to the mandrel. Axial movement of the mandrel 14 cooperates in controlling the volume of the cavity 37 as well as the pressure within the chamber.

The chamber 10 is vacuum formed by separately vacuum forming each of two polyvinyl sheets over a male die, and thereafter, nesting the formed sheets and RF (radio frequency) sealing the sheets along the peripheral edge or flange line. When a high-G port is desired, tubing is sealed in place between the sheets at the flange area and provides fluid communication with the cavity 37 via a high-G port.

When the chamber is distended, as suggested in Figure 2, the casing assumes a bladder-like configuration which may be referred to as a prolate ellipsoid. From the distended position, the top end of the inner wall 34 is depressed inwardly so as to form the depression which receives the mandrel 14.

In some situations, it is important at the end of the separation procedures to fully express all liquid from the processing chamber. This requires that the chamber walls be capable of being flattened against themselves and that the only space provided between the rotor bowl 12 and mandrel 14 will be about the thickness of the chamber's inner and outer walls.

As shown in Figure 3, the chamber material is sufficiently flexible at the rim area 40 that it can be folded back upon itself. Thus the inner wall 34 is folded back so that wall portions, such as 34a and 34b, contact each other and there is no space therebetween. The folded wall portions form the rim edge 34c.

As the bowl fills and empties, the rim edge 34c advances and retracts, and in a sense rolls, while retaining an edge. In Figure 3, the bowl is shown in an expanded position by the dashed lines with the inner wall 34 flattened against itself as it rolls axially upwardly and downwardly. Thus one of the inherent characteristics of the material selected for the inner wall is that it be capable of being folded flat against itself so as to define a rim area and rim edge and roll upwardly and downwardly without tearing or leaking.

Referring now to Figure 4, there are situations in which it is desirable to begin processing with an initial liquid volume in the chamber and/or to leave some liquid in the chamber at the end of the processing cycle. In such situations, the mandrel and rotor are arranged to permit the inner wall portions 34a and 34b to be spaced from each other in the rim area while still forming the rim edge 34c. The rim edge 34c advances upwardly and downwardly, but with the inner and outer walls spaced from each other. Again, the rim edge will not tear or leak.

In the simplest form, shown in Figure 1, only a single fluid port 38 is provided. Depending upon how the system is used, all fluid flow and separation can be accomplished through the port 38. Since the port is located on the spin axis, the port is referred to as the low-G (low-gravity) port. Alternatively, a single port could be provided at the greatest radial distance from the spin axis and this would be referred to as the high-G (high-gravity) port. In Figure 1, that position would be at the flange line 36. Other single port systems can be envisioned.

For some applications, multiple port systems are desirable. Referring now to Figure 2, the low-G port is shown as 38 and the high-G port as 42.

The high-G port is formed by bonding tubing between the inner and outer walls at the flange 36. The tubing connects the port to a Y-connector 43 or to a harness which holds the tubing connecting the low-G port 38. The connection between the rotating parts and stationary parts external of the rotor and chamber may be made in the manner disclosed in U.S. Patents Re. 29,738; 3,986,442; and 4,108,353.

A number of different processing techniques can be used for separating the therapeutic components using the rate of the spin, the mandrel and either one or two ports.

In some situations a three-port system may be desirable. In such a system a third port 44 is provided through the outer wall 32 at a position intermediate the low-G port 38 and high-G 42. The third port could be used as a blood inlet, so that blood entering at port 44 would immediately begin to separate with high density components (such as red blood cells) moving toward the high-G port 42 and the low density components (such as plasma) separating toward the low-G port 38.

This is but one technique to be used, and it is important to note that blood inlet port 44 can be provided through the side wall 32. If such a port were added, it could be connected via tubing to the Y-connector 43 adjacent port 38 in the same manner as the tubing from the high-G port 42.

The embodiment previously described is fabricated by the vacuum forming of two sheets and inclusion of molded ports and tubing. Another technique by which such a system can be prepared is by blow-molding in which, for example, the high-G port and return tubing are molded into the side wall.

One mode for operating the flexible volume reservoir is shown in diagrammatic form in Figures 5-12. Here for ease of consideration the variable-volume chamber is shown without the mandrel and rotor. It is understood that the chamber is held against the rotor wall and has assumed the shape of the rotor wall and mandrel.

In the system shown in Figure 5, the chamber 50 includes a low-G port 52 and line 53, and a high-G port 54 and line 56. The lines 53 and 58 are shown connected to a multiple-lumen umbilicus, which connects the low-G and high-G ports to external points. Various valves, clamps and pumps can be provided external of the chamber for controlling flow through the ports 52 and 54. One such system is described hereinafter.

As shown in Figure 5, the mandrel has compressed the chamber so that the chamber's inner and outer walls are compressed together.

Initially a small amount of anticoagulant is metered into the processing chamber (or is provided at the time of manufactured), and as shown in Figure 6, whole blood is delivered to the chamber and enters via low-G port 52. The blood fills the chamber and mixes with the anticoagulant. As the blood enters the chamber, the rotor rotates slowly and the mandrel retracts so as to fill the chamber with about 525 milliliters of whole blood.

Thereafter, the processing apparatus spins the rotor, chamber and mandrel in a first spin so as to separate the blood into red blood cells (RBC) and platelet-rich plasma (PRP). This spin is sometimes referred to as a soft spin and the specific spin conditions, as is known in the art, depend on factors such as rotational velocity, bowl surface area, time, initial blood hematocrit, and the like.

Referring now to Figure 7, the red blood cells (RBC) move radially outwardly along the sides of the chamber, and the platelet-rich plasma collects in the center portion of the chamber and is identified as PRP. Red blood cells may be collected by closing the low-G port 52, opening the high-G port 54, and moving the mandrel downwardly so that the volume of the processing chamber is reduced, and red blood cells are forced from the chamber through the high-G port 54 and line 58 for harvesting and collection. This leaves the platelet-rich plasma (PRP) in the flexible bowl as shown in Figure 8.

Referring now to Figure 9, the bowl is than subjected to a second spin which separates the platelets from the platelet-rich plasma by driving the platelets along the outer wall, which leaves the platelet-free plasma at the center. This is sometimes known as a hard spin. Thereafter, the high-G port 54 is closed, the low-G port 52 is opened, the mandrel is moved downwardly, and the platelet-free plasma (PRP) is expressed from the chamber, as shown in Figure 10.

The mandrel is then retracted, which draws a small amount of air into the system from an empty but sterile and closed transfer pack or collection bag. Agitation resuspends the platelets into a small volume of carrier plasma. Under a third spin, or soft spin, as shown in Figure 12, the mandrel expresses the platelet concentrate out of the chamber and into a collection bag for transporting. Alternatively, the platelets can be transported in the processing bowl rather than being collected and transported in a separate bag.

As can be seen from these drawings, the volume of the chamber varies as blood is introduced into the chamber and in accordance with the separation procedure which is being used. In so doing, the rim edge 34c moves upwardly and downwardly, and thus that area must be flexible as previously described.

In an alternative embodiment, the outer wall of the chamber may be rigid and a predetermined portion of the inner wall may be rigid. But the rim area and the rim edge must remain flexible.

A complete, integral, disposable, sterile and sealed collection and separation system is shown in Figure 13. This entire system is sterilely sealed upon manufacture and, as such, can be used to store and transport whole blood and components for times greater than those permitted by regulation when the system is open or pierced in the field.

In this system the flexible, variable-volume processing chamber 60 includes a high-G port 62 and tubing 64 and a low-G port 66 and tubing 68. The tubing may be threaded through peristaltic roller pumps 70 and 72 and then connected at a Y-junction 74. It will be recalled that the chamber 60 is rotating while the pumps 70 and 72 are fixed in place.

The rotating chamber and stationary pumps are connected via tubing 64 and 68. This connection is made in accordance with the teaching of U.S. Patents Re. 29,738; 3,986,442; and 4,108,353, which permit a sealless connection between rotary and stationary members. This fluid communication is established without rotary seals or the like.

The tubing 76 leading from junction 74 connects to a standard red blood cell collection bag 78, a standard plasma collection bag 80, a special breathable platelet collection bag 82, a saline-containing bag 84, an anticoagulant bag 85, and a catheter 86. Anticoagulant can be provided from a separate bag as shown or may be initially provided in the processing chamber 60 in which case an anticoagulant bag, such as 85, is not included the system.

With this system the saline solution may be drawn from bag 84 and anticoagulant from bag 85, through line 76, and into the chamber 60 for priming. Thereafter, blood is taken from the patient

via catheter 86 and delivered via line 76 to chamber 60, preferably through low-G port 62. During this phase, the collection bags may be clamped using external clamping means, such as forceps or hemostats.

Various separation procedures have been described above, and as can be seen, red blood cells, for example, may be drawn from the high-G port 62 utilizing roller pump 70 and delivered to the red blood cell collection bag 78. Next, platelet-free plasma may be drawn from the low-G port 66 using pump 72 and delivered to the plasma collection bag 80. Then platelet concentrate may be collected via high-G port 62, pump 70 and delivered to the special platelet collection bag 82.

It will be understood that the entire system is disposable and sterilely sealed at the plant. Thus, it may be removed from the centrifuge, from the roller pumps 70 and 72, from the patient 86 and delivered to the processing site.

A preferred embodiment of the processing chamber is shown in Figures 14 through 17, being therein identified by reference numeral 112. As shown, the chamber 112 includes an inner wall 116 and an outer wall 118. These walls form a bowl-shaped chamber having a generally cylindrical bottom section 120 and a generally annular upstanding side wall section 122.

Referring now to Figure 15, it is seen that the bottom section 120 is formed by the transverse bottom wall portions of the inner wall 116a and of the outer wall 118a. The side wall portions are formed by the upstanding side wall 116b of inner wall and upstanding side wall 118b of the outer wall.

The inner wall 116 and outer wall 118 form a flexible rim area 124 which flexes and appears to roll as the chamber volume increases and decreases, thereby permitting changes without tearing or rupturing. The walls are each formed from a flexible

polyvinylchloride sheet which is vacuum formed and the sheets are then heat sealed along a peripheral flange 126 so as to form the sealed chamber.

As shown in Figure 14, a high-gravity port 128 is formed in the flange at the radially outermost point and a low-gravity port 130 is formed in the bottom wall at the intersection of the spin axis A-A. Conduits 132 and 134 connect the ports 128 and 130 to external blood sources and collection containers. The chamber 112 is fitted into the bowl cover 110 and tubing from the chamber ports its within slot 129. A chamber engaging mandrel 114 is also provided as heretofore described. Stationary seal connections are made to the external blood sources and collection points as shown in U.S. Patents 4,151,844; 4,285,464; and 4,389,207.

Referring again to Figure 15, when the chamber is filled, it expands and the inner bottom wall portion 116a moves upwardly away from the bottom wall portion 118a, the inner side wall 116b moves inwardly from the outer wall 118a, and the rim area 124 moves axially upwardly.

The space between the bottom walls forms a cylindrical or disc-like plasma processing volume (Vp) 36, which has an outer cylindrical surface 138. The space between the side wall forms an annularly shaped red blood cell processing volume (Vbc) 40.

The interface between the blood volume and plasma volume is along the cylindrical surface 138, which forms at the transition from the bottom to the side wall. The bowl is shaped so that when blood having a hematocrit between 40-60 (ie., volume percent red blood cells) is processed, the red blood cell volume 40 and plasma volume 36 are approximately equal whether the bowl is fully filled as in Figure 15 or partially filled as in Figure 16.

The bowl is also constructed such that the red blood cell sedimentation surface area (S_1) 118b is greater than the interface surface area (S_2) 132. For example, when the bowl is fully filled, the red blood cell sedimentation surface area 118b may be about four times that of the interface 138.

When the bowl is partially filled, as seen in Figure 16, the red blood cell area (S_1) 118b is clearly greater than the interface surface area (S_2) 138.

In operation, whole blood is introduced into the chamber through the low-G port 130, for example, and the apparatus is spun about the axis A-A in a first or hard spin. During this first spin the heavier red blood cells are driven toward or sediment against the outer wall 118b and red blood cells fill the blood cell volume 40. Platelet-rich plasma in the volume 40 is displaced inwardly toward the plasma volume 36. Eventually the red blood cells, which are experiencing high gravity forces, sediment or "pack out", thus filling the volume 40. Using this procedure, platelet separation from the red blood cells is maximized as is red blood cell purity.

The plasma volume 36 fills with the platelet-rich plasma initially in the volume and with the platelet-rich plasma displaced into the volume. The platelet-rich plasma in the plasma volume 36 experiences low-G forces as compared to the forces experienced by the red blood cells. The plasma at the axis A-A experiences almost no centrifugal forces, and the plasma at the interface 138 experiences some centrifugal forces.

Due to displacement and centrifugal forces some platelets will separate from the plasma and form a buffy layer at the interface 120. However, the amount of platelet separation and buffy layer formation is minimized and is related to the spin rate, plasma viscosity, interface position, and the like. The intent is to minimize platelet separation and buffy layer formation during red blood cell separation.

In one example, the chamber was fully filled with about 500 milliliters of whole blood which has a hematocrit of about 40 (ie., 40 volume per cent red blood cells).

After the first or hard spin, the red blood cells formed a bed of packed cells in the volume 40, platelet-rich plasma collected in volume 36, and a thin buffy layer formed at interface 138. The packed cell volume was about 250 milliliters and the plasma volume was about 250 milliliters.

It will be appreciated that due to the higher G forces and larger surface area, the red blood cells separated or sedimented faster than the platelets at the interface 138.

After separation, the red blood cells can be collected through the high-G port 128 with minimal platelet contamination. Thereafter, the chamber can be utilized for platelet/plasma separation.

Since the volume relationships remain substantially constant (ie., about equal) and the red blood cell sedimentation area is greater than the buffy layer area, small or large quantities of whole blood can be processed.

Figure 16 shows the variable volume chamber set to process less than 525 milliliters of whole blood. As in Figure 15, the volumes are about equal and the red blood cell surface area is greater than the interface area. Processing is performed in substantially the same manner and the same type of separation is effected.

In Figure 17, an enclosed, rigid, fixed volume processing bowl 150 is shown. The housings, drives and controls for operating a rigid bowl system are known in the art. The bowl 150 may be blow-molded or fabricated from plastic members and includes rigid inner and outer walls 152 and 154 which define a fixed internal volume that includes a red blood cell volume 56 in the side wall and a plasma volume 58 in the bottom wall. The bowl includes a red

blood cell sedimentation surface 160 and is structured to permit a buffy layer or interface 162 to form and be defined. High-G and low-G ports 164 and 166 and related conduits are also provided. Separation of therapeutic components using this bowl is similar to separation using the variable volume bowl except that no volume variation occurs.

It will be appreciated that numerous changes and modifications can be made to the embodiments disclosed herein without departing from the spirit and scope of this invention.

CLAIMS:

1. A flexible, variable-volume, bowl-shaped chamber for use in centrifugal apheresis for receiving whole blood, separating blood into therapeutic components, and selectively collecting therapeutic components of blood, said chamber comprising:

an enclosed bladder-like casing which is formable into said bowl-shaped chamber, said chamber having a bowl-shaped outer wall, and a bowl-shaped inner wall positioned within said outer wall which defines a blood processing cavity therebetween and a flexible rim area connecting said inner wall and outer wall, which area defines a rim edge;

said flexible rim area being adapted to fold against itself to form a rim edge which is adapted to advance and retract as said chamber volume changes; and

said outer wall having at least one port extending therethrough for fluid communication with the blood-processing space.

2. A variable-volume chamber as in Claim 1, wherein a pair of ports are provided, with one port passing through the outer wall at the central spin axis to form a low-gravity port and the other port passes through the casing at a radially outermost point so as to form a high-gravity port.

3. A variable-volume chamber as in Claim 2 wherein a third port is provided, which passes through the outer wall at a point intermediate the low-gravity and high-gravity ports.

4. A variable-volume chamber as in Claim 1, wherein said inner and outer walls at said rim area are spaced from each other and are constructed to move in axially opposite directions as said chamber is filled and emptied so that the rim edge appears to roll axially.

5. A variable-volume chamber as in Claim 1, wherein said inner and outer walls at said rim area contact each other and slide against each other in opposite directions as said chamber is filled and emptied so that the rim edge appears to roll axially.

6. A variable-volume chamber as in Claim 1, wherein said chamber forms a part of a disposable blood collection and component separation system which comprises said chamber, at least one therapeutic component collection container integrally and sterilely connected to at least one port of said bowl-shaped chamber, and catheter means integrally and sterilely connected to said bowl-shaped chamber to at least one port of said bowl-shaped chamber.

7. A system as in Claim 6, wherein there is provided three component collection containers, each adapted and constructed to receive a therapeutic component; one of said containers adapted to receive red blood cells; a second to receive platelets; and a third for receiving platelet-free plasma, each of said collection containers being constructed to be selectively opened and closed to receive a component from said processing chamber.

8. An enclosed processing bowl for use in centrifugal apheresis, said bowl having inner and outer walls which define a bottom section, a side wall section, and a blood-receiving cavity between said walls and at least one port for fluid communication with said cavity, and said bowl having a spin axis extending centrally through said bowl;

the bottom section of the bowl defining a cylindrically-shaped plasma processing volume between the inner and outer walls of said bottom;

the side wall section of the bowl defining an annularly-shaped red blood cell processing volume between the inner and outer walls of said side wall;

said plasma processing volume and red blood cell processing volume being adjacent each other at the transition from the bottom wall to the side wall to form a generally cylindrical interface;

said outer wall of said annularly-shaped red blood cell processing volume forming a red blood cell sedimentation surface; and

the surface area of the red blood cell sedimentation surface being greater than the area of the cylindrical blood cell plasma interface.

9. A centrifugal processing bowl as in Claim 8, wherein the bowl is substantially symmetric about said spin axis.

10. A centrifugal processing bowl as in Claim 8, wherein the volume of the red cell processing volume and volume of the plasma processing volume are substantially equal.

11. A centrifugal blood processing bowl as in Claim 8, wherein the red cell processing sedimentation surface area is at least twice the surface area of the interface.

12. A centrifugal blood processing bowl as in Claim 11, wherein the red cell processing sedimentation surface area is about four times greater than the surface area of the interface.

13. A centrifugal blood processing bowl as in Claim 8, wherein said bowl is of a fixed volume and the inner and outer walls are fixed and rigid.

14. A centrifugal blood processing bowl as in Claim 8, wherein said bowl is of a variable volume and the inner and outer walls join at a rim area and at least the rim area of said bowl are flexible so as to accommodate changes in bowl volume.

15. A centrifugal blood processing bowl as in Claim 14, wherein the red cell processing volume and plasma volume are approximately equal and said volumes remain equal to each other throughout the range of chamber column changes from empty to full.

FIG. 1

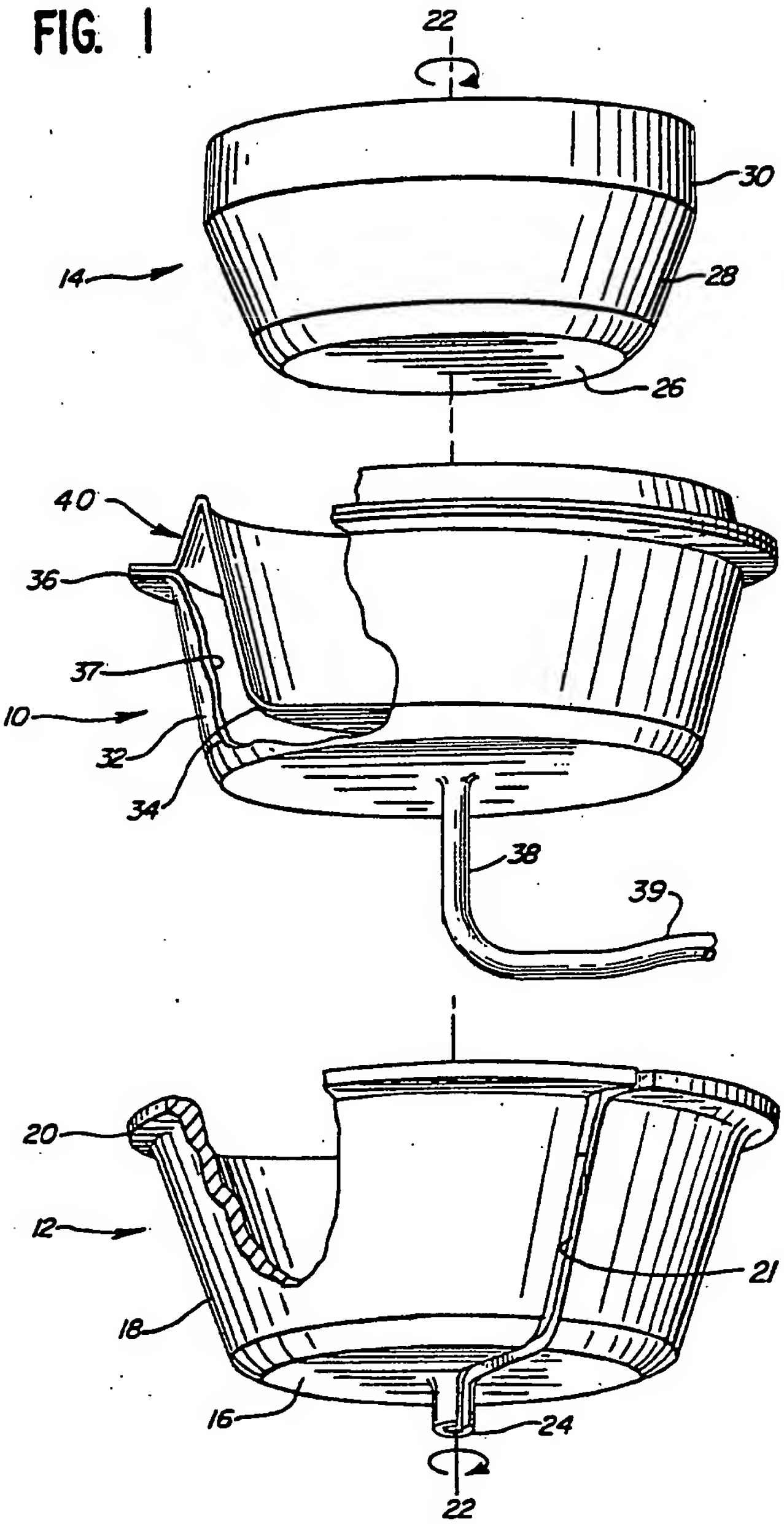


FIG. 2

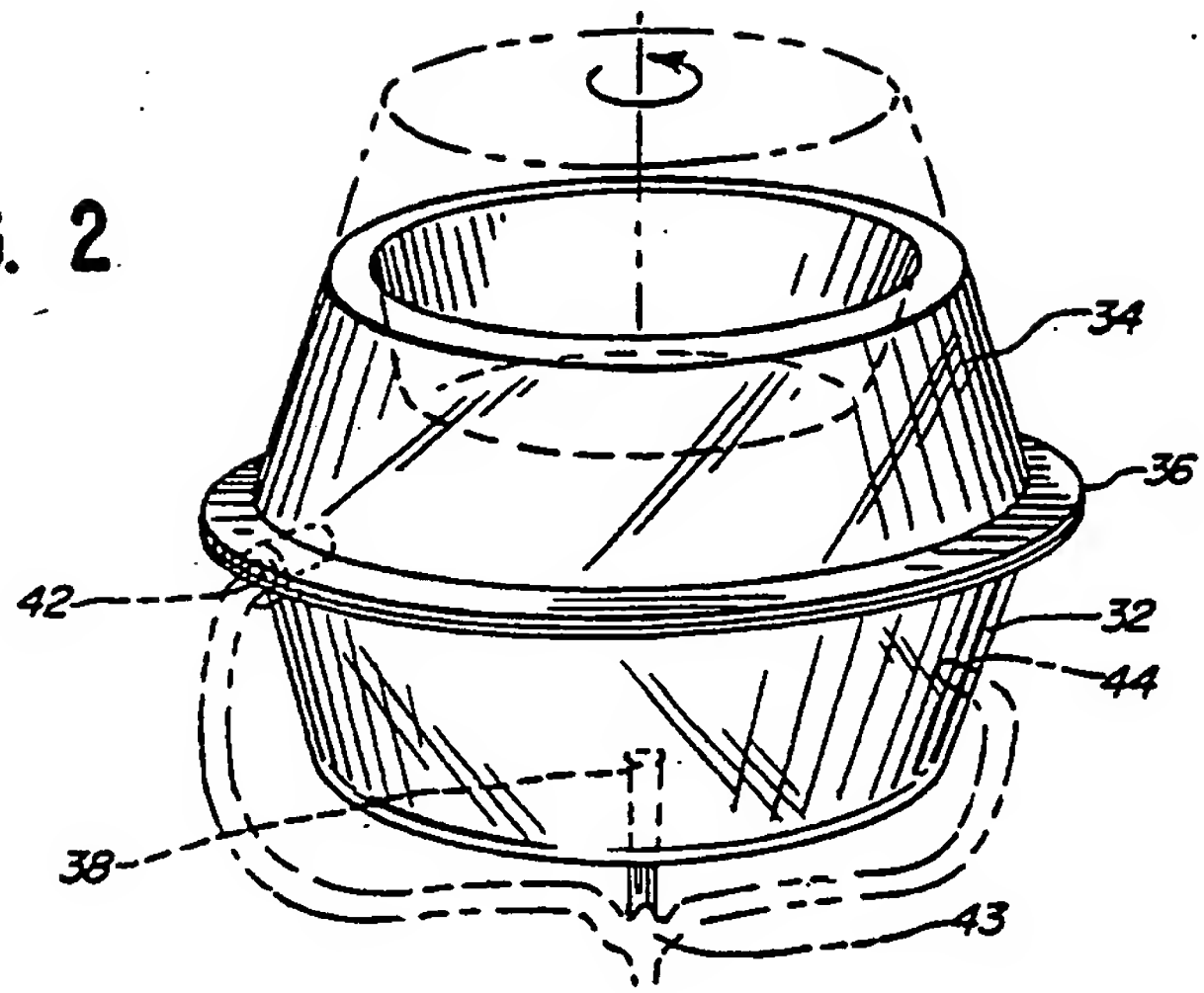


FIG. 3

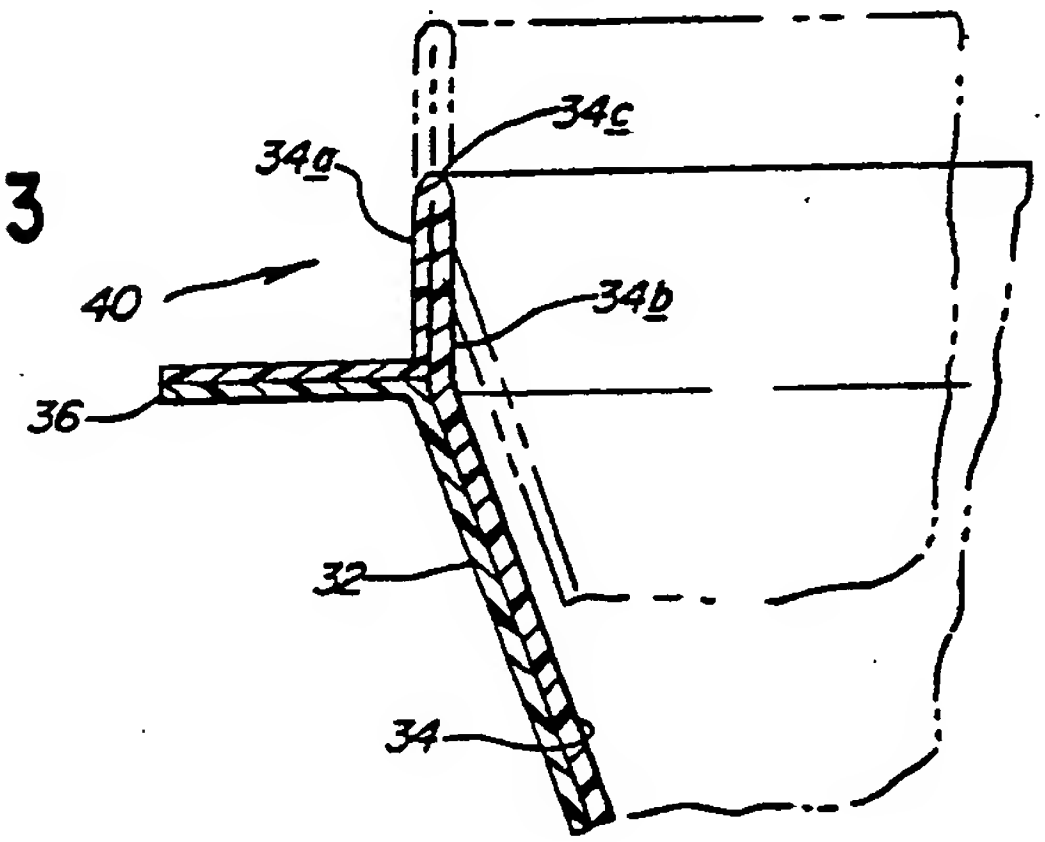
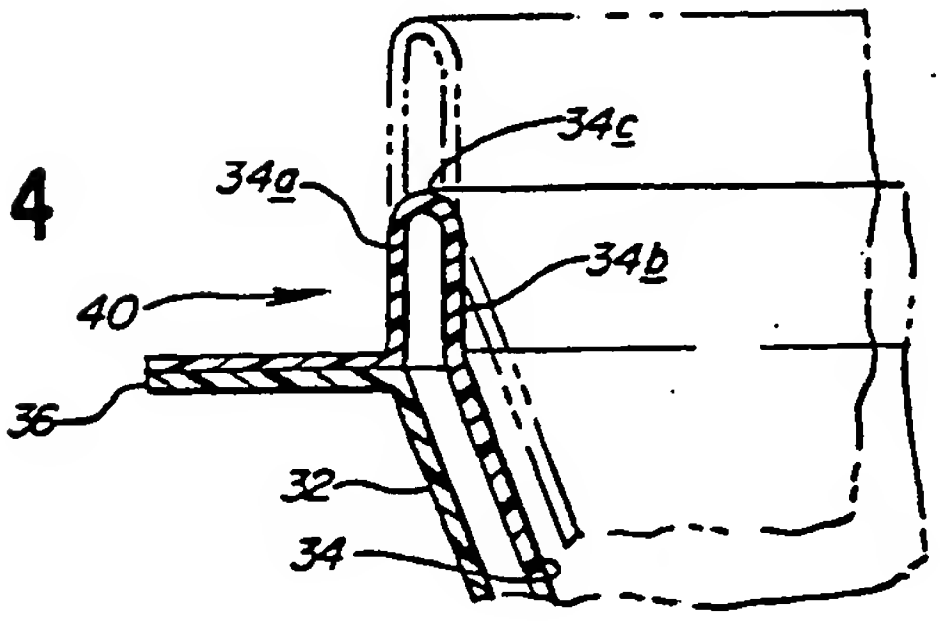


FIG. 4



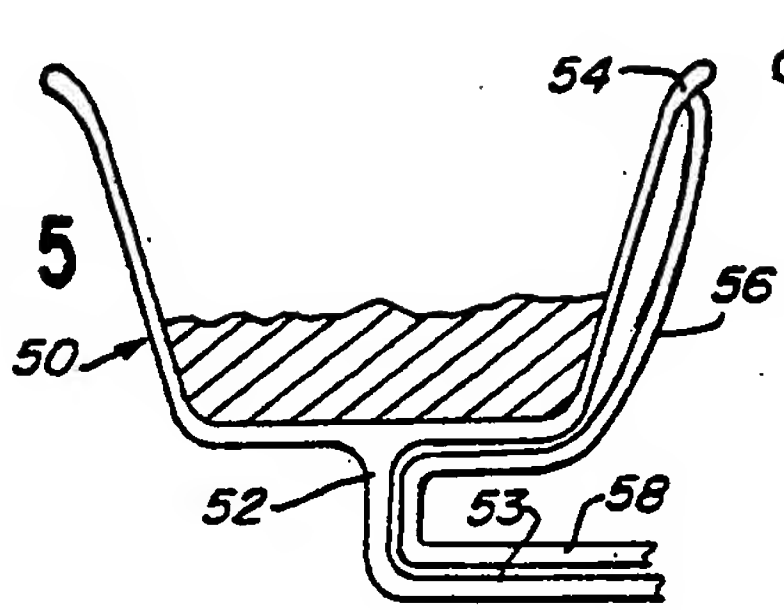


FIG. 5

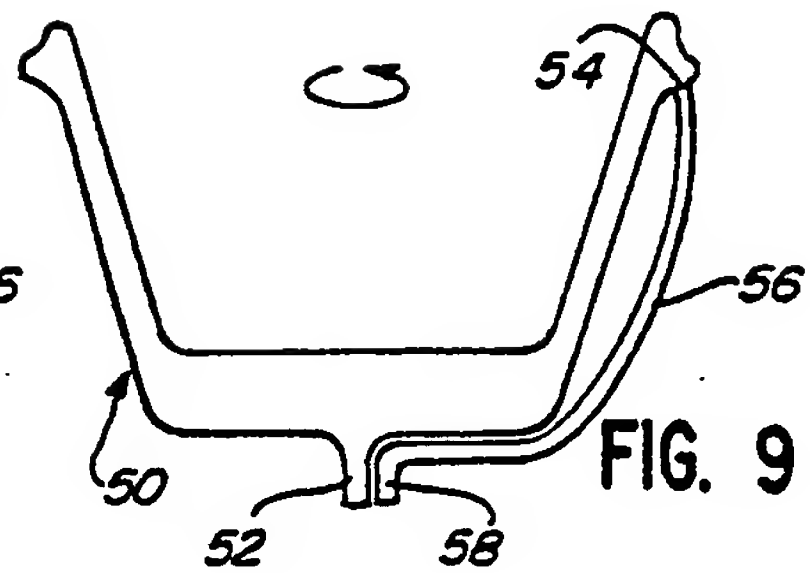


FIG. 9

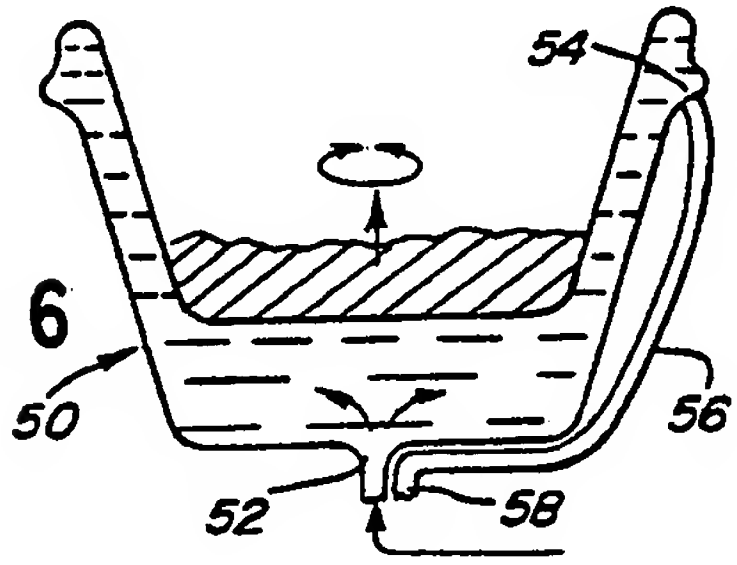


FIG. 6

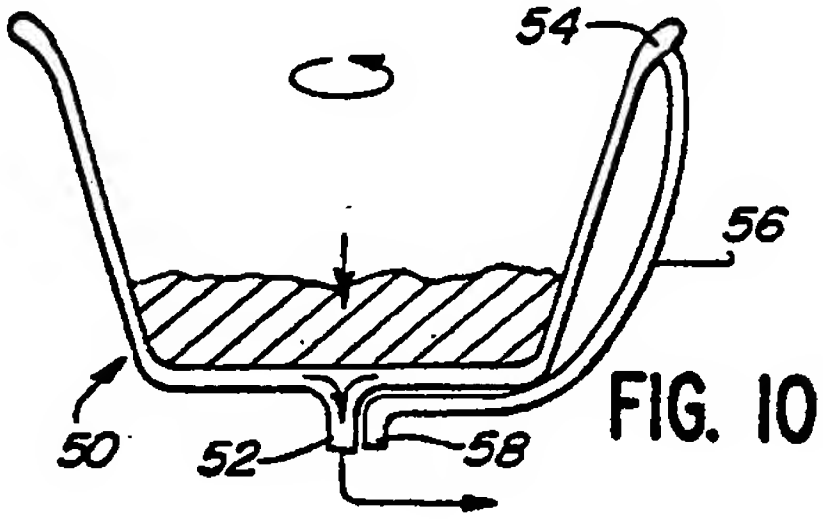


FIG. 10

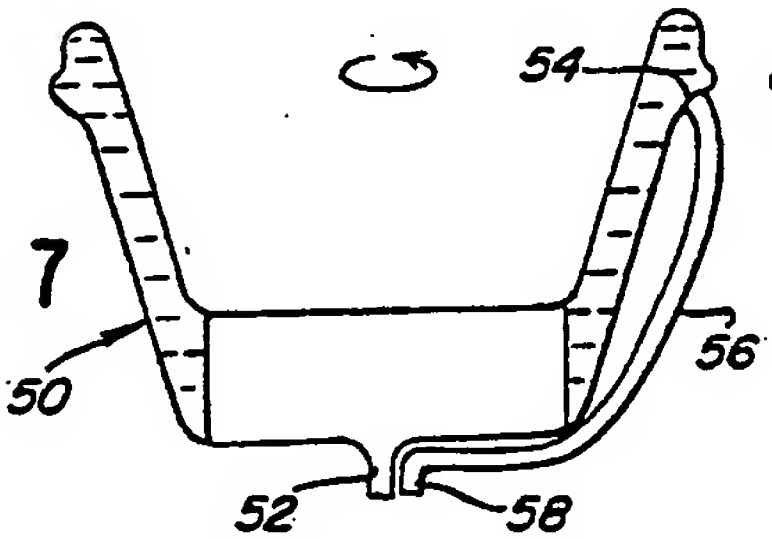


FIG. 7

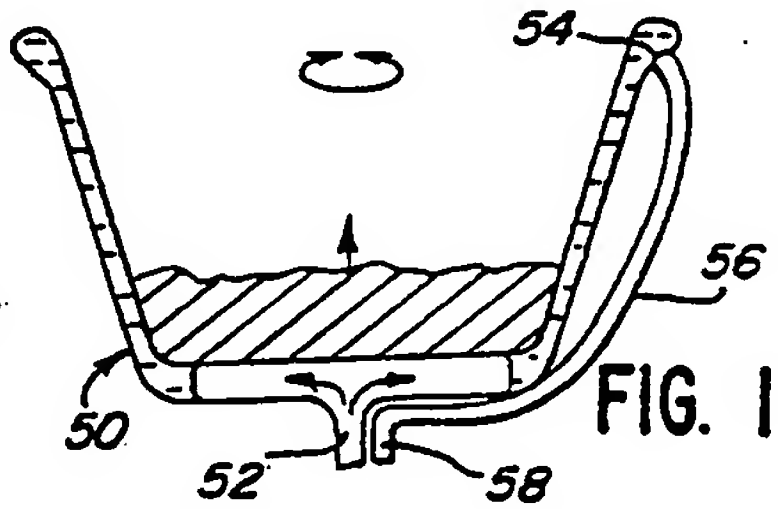


FIG. 11

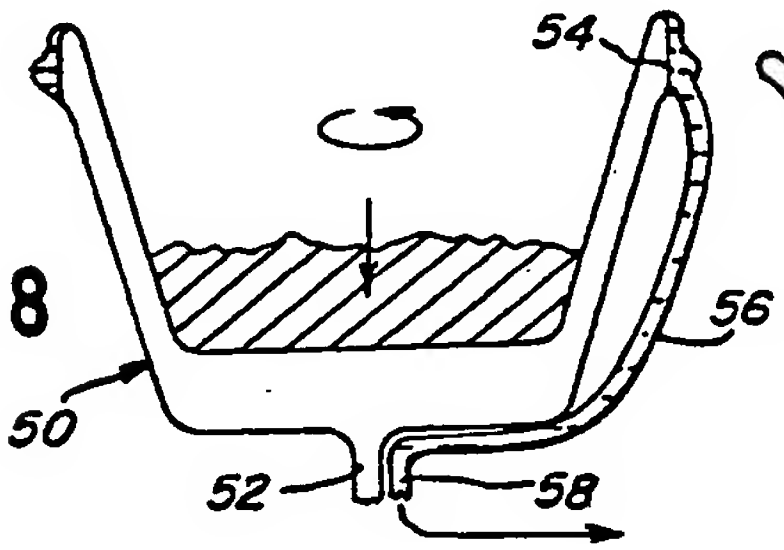


FIG. 8

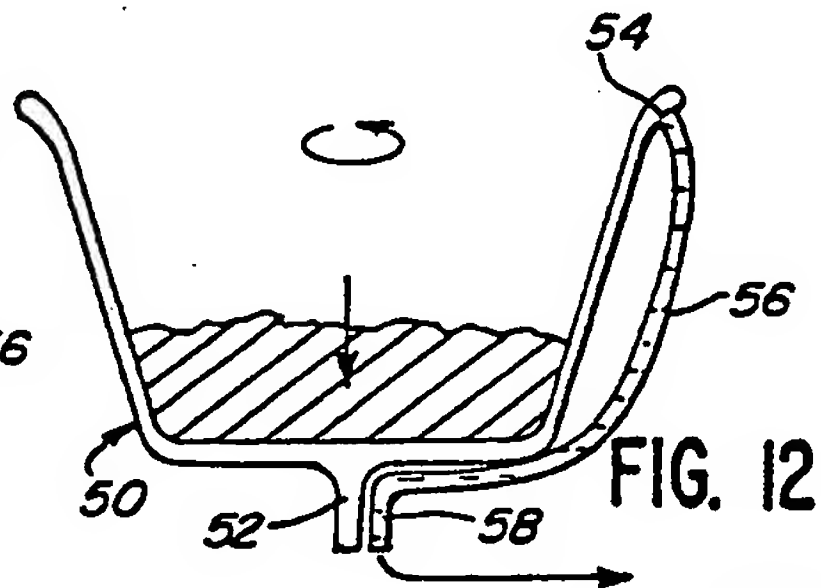


FIG. 12

FIG. 13

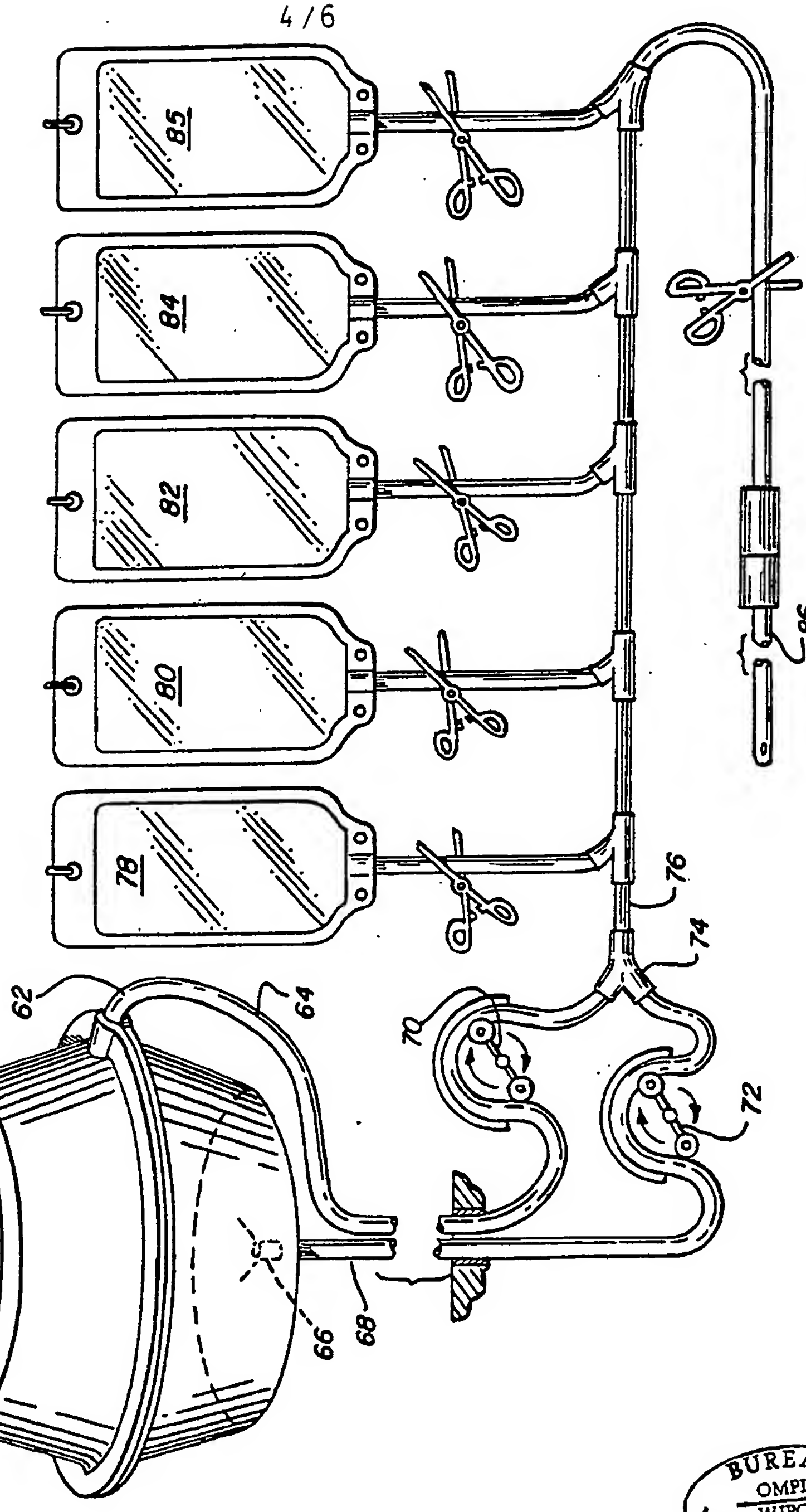
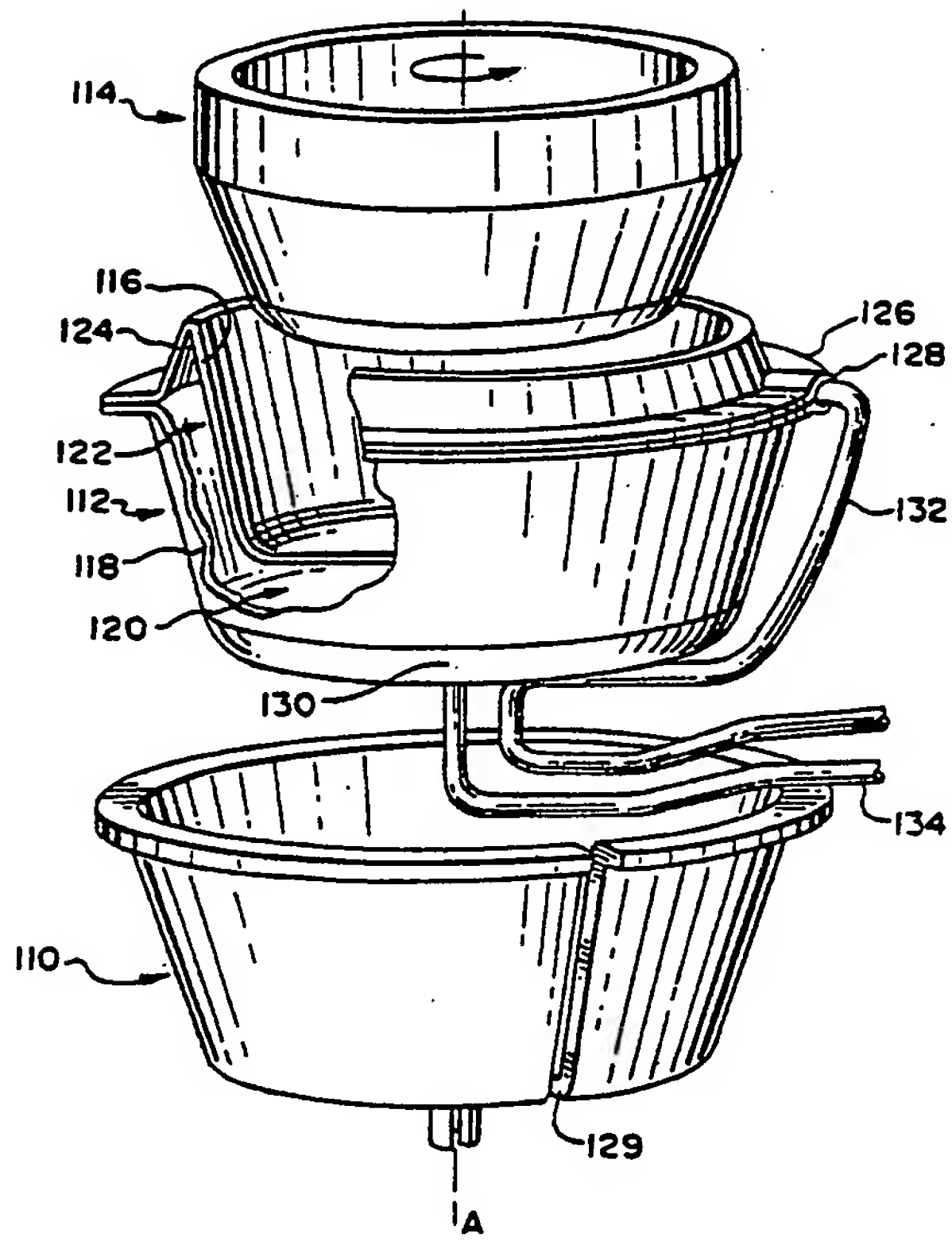


FIG. 14



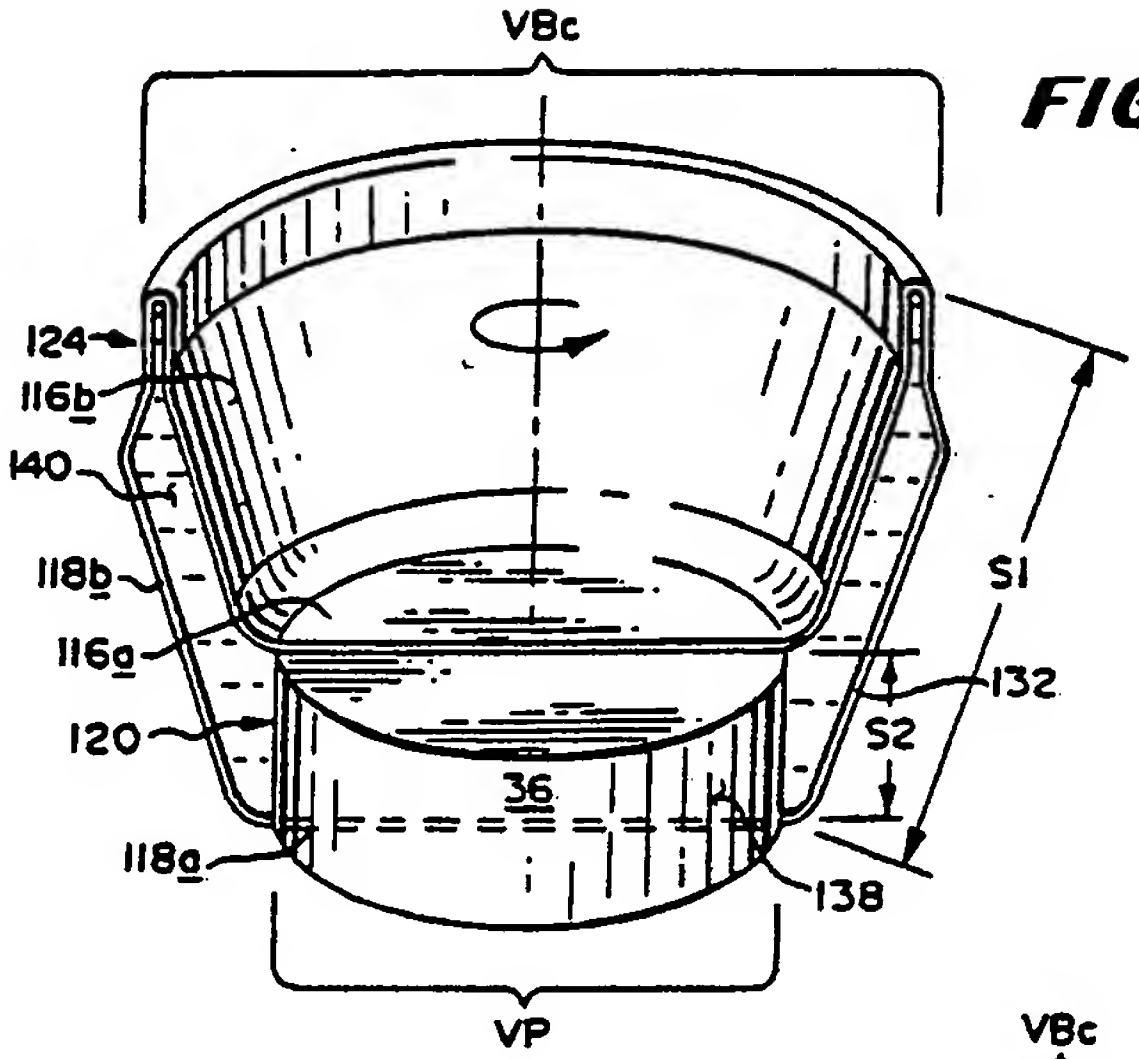


FIG. 15

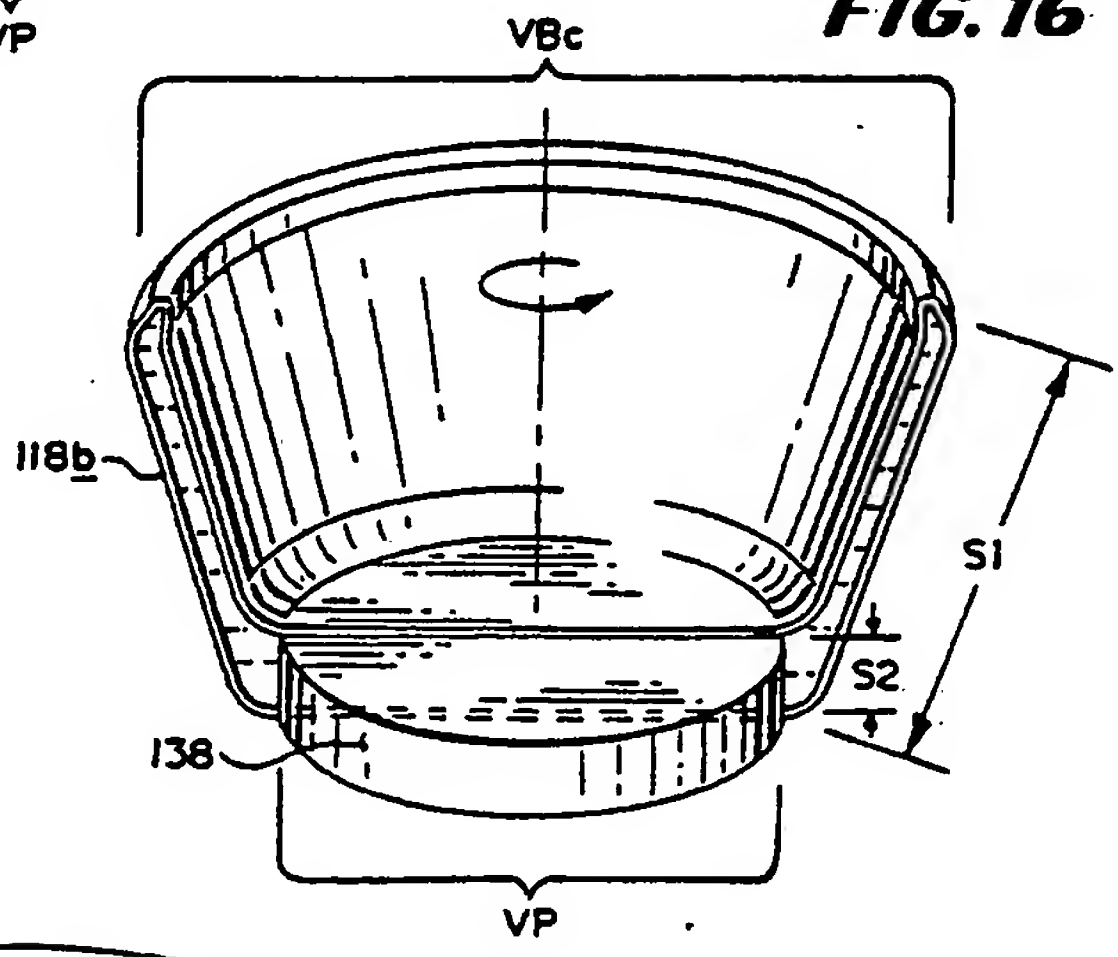
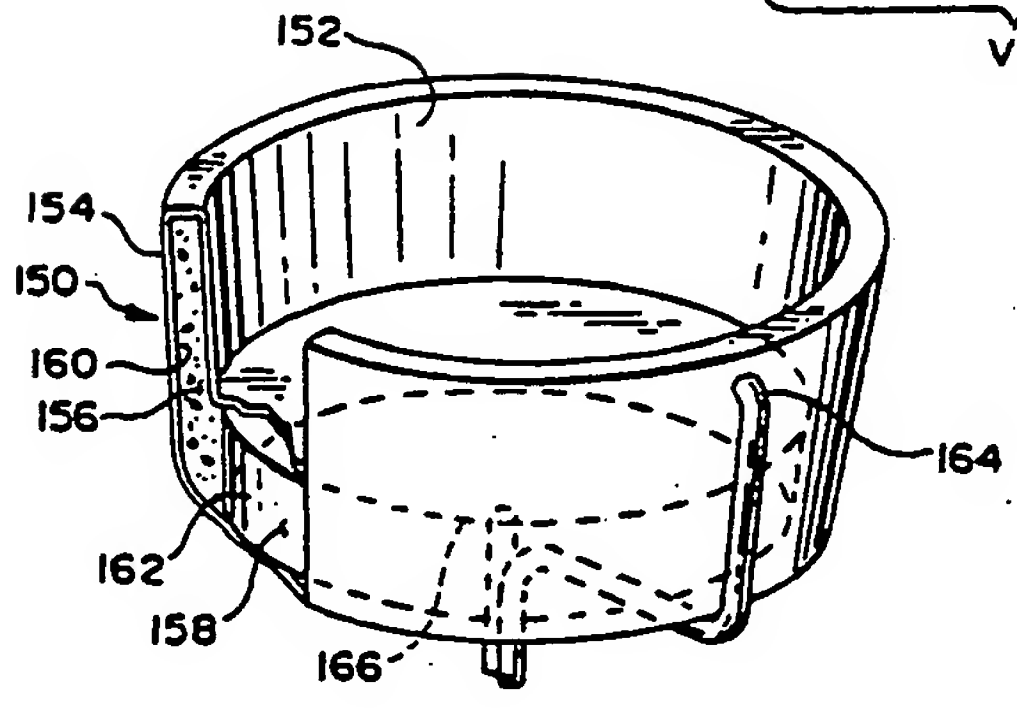


FIG. 16

FIG. 17



INTERNATIONAL SEARCH REPORT

PCT/US84/01795

International Application No

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) [3]

According to International Patent Classification (IPC) or to both National Classification and IPC

INT. CL. B04B 1/10, 1/12, 11/02
U.S. CL. 494/45,65 ; 210/512.1, 787,927

II. FIELDS SEARCHED

Minimum Documentation Searched [4]

Classification System	Classification Symbols
U.S.	494/18,20,21,45,65,84 210/512.1,787,927 604/4-6,408

Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched [5]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [14]

Category *	Citation of Document, [16] with indication, where appropriate, of the relevant passages [17]	Relevant to Claim No. [18]
Y	US, A, 4,413,771, PUBLISHED 08 NOVEMBER 1983, ROHDE ET AL.	1-7, 14,15
Y	US, A, 4,413,772, PUBLISHED 08 NOVEMBER 1983, ROHDE ET AL.	1-7, 14,15
Y	US, A, 4,413,773, PUBLISHED 08 NOVEMBER 1983, ROHDE ET AL.	1-7 14,15
Y	US, A, 4,151,844, PUBLISHED 01 MAY 1979, CULLIS ET AL.	1-15
Y	US, A, 3,244,363, PUBLISHED 05 APRIL 1966, HEIN.	1-7, 14,15
A	US, A, 3,145,713, PUBLISHED 25 AUGUST 1964, LATHAM, JR.	1-15
A	US, A, 3,858,796, PUBLISHED 07 JANUARY 1975, UNGER ET AL.	1-15
A	US, A, 3,987,961, PUBLISHED 26 OCTOBER 1976, SINN ET AL.	1-15

* Special categories of cited documents: [15]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search [2]

14 DECEMBER 1984

Date of Mailing of this International Search Report [2]

28 DEC 1984

International Searching Authority [1]

ISA/US

Signature of Authorized Officer [20]

JOHN DONOFRIO

Form PCT/ISA/210 (second sheet) (October 1981)